C5
Cont

90. A filamentous bacteriophage comprising the processed gVIII fusion protein of claim 89 expressed on its surface.

---

**REMARKS**

Claims 1 and 88-91 are presently pending and under examination.

The specification has been amended to correct the typographical errors at pages 29 and 57 as well as the legends to Figures 3 and 5-10 objected to in the current Office Action at page 2 in the paragraph designated "Specification."

Claim 89 has been amended herein to correct typographical and punctuation errors. Claim 90 has been amended to recite a "processed gVIII fusion protein" in order to clarify the antecedent basis in claim 89.

The amendments to the specification and claims do not raise an issue of new matter and entry thereof is respectfully requested. Furthermore, in light of these amendments, Applicant respectfully requests that the objections to the disclosure and claims set forth at page 2 of the current Office Action be withdrawn.

Applicant has set forth above the amendments to the claims and specification in clean form as required under 37 C.F.R. § 1.121(c)(1)(i) and 37 C.F.R. § 1.121(b)(1)(i) and (ii).

Applicant also attaches Appendix A with marked up amendments indicated with brackets and underlining as required under 37 C.F.R. § 1.121(c)(1)(ii) and 37 C.F.R. § 1.121(b)(1)(iii).

**Regarding the Rejection under 35 U.S.C. §112, Second Paragraph**

Applicant respectfully traverses the rejection of claims 90 and 91 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to point out and distinctly claim the subject matter regarded as the invention.

Applicant respectfully submits that claims 90 and 91 are clear and definite to the skilled person in view of the specification and that which was known in the art at the time the present application was filed.

With regard to claim 90, the Examiner suggests at page 3, third paragraph, of the current Action (Paper No. 7) that recitation of the term "processed gVIII fusion protein" rather than "gVIII fusion protein" would overcome the rejection. Applicant has amended claim 90 herein to recite "processed gVIII fusion protein" rather than "gVIII fusion protein." Applicant therefore respectfully requests removal of the rejection of claim 90 under 35 U.S.C. §112, second paragraph, as allegedly indefinite.

With regard to claim 91, the Examiner asserts that the phrase "or modification thereof" renders the metes and bounds of the claim indeterminate. Applicant respectfully submits that

the phrase "or modification thereof" is clear and definite to the skilled person in view of the specification and that which was known in the art at the time the present application was filed.

> Determining whether a claim is definite requires an analysis of 'whether one skilled in the art would understand the bounds of the claim when read in light of the specification.' If the claims read in light of the specification reasonably apprize those skilled in the art of the scope of the invention, section 112 demands no more.

Personalized Media Communications, LLC v. Int'l Trade Comm'n, 161 F.3d 696, 705 (Fed.Cir. 1998) (quoting Miles Lab., Inc. v. Shandon, Inc., 997 F.2d 870, 875 [Fed.Cir. 1993]). The focus of the inquiry, then, is on the clarity of the claim terms and the extent to which such terms, viewed from the perspective of one of ordinary skill in the art, sufficiently identify the actual invention. Personalized Media, 161 F.3d at 705.

The specification teaches that minor modifications can be introduced into proteins so long as the function of the protein is retained. For example, the specification describes the inclusion of additional amino acids such as the peptide linker sequence attached to the amino-terminus of the functional portion of gVIII (see, for example, page 41, lines 26-29).

Other minor sequence modifications are also taught in the specification, for example, the deletion of a GCC codon in the leader sequence of the fusion protein sequence does not alter

the function of the leader or of the processed gVIII fusion protein (page 62, lines 11-15). In addition, mutation of the leader sequence was performed to increase secretion of the product. The substitution of an A for a G within a codon of the leader allowed function to be maintained (page 65, lines 23-24 and lines 24-26). Also, removal of the amber codon between the peptide and gene VIII fusion resulted in retention of function, indicating that the presence of the amber codon was not required (page 67, lines 6-11). Therefore, the specification sufficiently teaches that minor sequence modifications and conservative substitutions can be introduced while still maintaining function.

Applicant has exemplified the use of a pseudo-wild type gVIII sequence which is not identical to the wild type sequence because it is truncated at its amino terminus. The specification thus teaches that it is unnecessary for the non-identical pseudo-wild type gene to encode a sequence identical to a wild type amino acid sequence so long as the pseudo-wild type gVIII gene encodes a functional portion of gVIII which causes expression of the gVIII fusion protein on the surface of a filamentous bacteriophage. Overall, Applicant maintains that the specification provides sufficient guidance to render clear and definite to one of ordinary skill in the art the metes and bounds of the term "modification" to sufficiently identify Applicant's actual invention as defined by claim 91.

Accordingly, Applicant respectfully requests that the Examiner remove the rejection of claim 91 under 35 U.S.C. §112, second paragraph, as allegedly indefinite.

**Regarding the Rejections under 35 U.S.C. §102(e)**

Claims 88-91 stand rejected under 35 U.S.C. §102(e) as allegedly anticipated by United States Patent No. 5,403,484, to Ladner et al. Applicants respectfully request that this rejection is held in abeyance until there is an indication of allowable subject matter in the subject application.

**Regarding Obviousness-Type Double Patenting**

Claim 1 stands rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 29 of U.S. Patent No. 6,258,530. Applicants respectfully request that this rejection is held in abeyance until there is an indication of allowable subject matter in the subject application.

**CONCLUSION**

In light of the Amendments and Remarks herein, Applicant submits that the claims are now in condition for allowance and respectfully requests a notice to this effect.

Should the Examiner have any questions, she is invited to call Cathryn Campbell or the undersigned attorney.

Respectfully submitted,

August 22, 2002
Date

Astrid R. Spain
Registration No. 47,956
Telephone No. (858) 535-9001
Facsimile No. (858) 535-8949

CAMPBELL & FLORES LLP
4370 La Jolla Village Drive
7th Floor
San Diego, California 92122
**USPTO CUSTOMER NO. 23601**

**Attachments:**

Appendix A Marked up version of specification and claims reflecting amendments.

Inventor: William D. Huse
Serial No.: 09/727,311
Filed: November 29, 2000





**APPENDIX A**

In the specification:

Page 4, Figure 3 legend:

[Figure 3 is a] Figures 3A through 3E show schematic diagrams of the two vectors used for sublibrary and library production from precursor oligonucleotide portions. M13IX22 (Figure 3A) is the vector used to clone the anti-sense precursor portions (hatched box). The single-headed arrow represents the lac p/o expression sequences and the double-headed arrow represents the portion of M13IX22 which is to be combined with M13IX42. The amber stop codon for biological selection and relevant restriction sites are also shown. M13IX42 (Figure 3B) is the vector used to clone the sense precursor portions (open box). Thick lines represent the pseudo-wild type ( gVIII) and wild type (gVIII) gene VIII sequences. The double-headed arrow represents the portion of M13IX42 which is to be combined with M13IX22. The two amber stop codons and relevant restriction sites are also shown. Figure 3C shows the joining of vector population from sublibraries to form the functional surface expression vector M13IX. Figure 3D shows the generation of a surface expression library in a non-suppressor strain and the production of phage. The phage are used to infect a suppressor strain (Figure 3E) for surface expression and screening of the library.

Pages 4-5, legends corresponding to Figures 5 through 10:

Figures 5-1 and 5-2 depict [is] the nucleotide sequence of M13IX42 (SEQ ID NO: 1).

Figures 6-1 and 6-2 depict [is] the nucleotide sequence of M13IX22 (SEQ ID NO: 2).

Figures 7-1 and 7-2 depict [is] the nucleotide sequence of M13IX30 (SEQ ID NO: 3).

Figures 8-1 and 8-2 depict [is] the nucleotide sequence of M13ED03 (SEQ ID NO: 4).

Figures 9-1 and 9-2 depict [is] the nucleotide sequence of M13IX421 (SEQ ID NO: 5).

Figures 10-1 and 10-2 depict [is] the nucleotide sequence of M13ED04 (SEQ ID NO: 6).

Page 29, lines 21-22:

[Isolation and Characterization of Peptide Ligands Generated From Right and Left Half Random Oligonucleotides] Isolation and Characterization of Peptide Ligands Generated From Right and Left Half Random Oligonucleotides

Page 57, lines 2-4:

[Isolation and Characterization of Peptide Ligands Generated From Oligonucleotides Having Random Codons at Two Predetermined Positions]Isolation and Characterization of Peptide Ligands Generated From Oligonucleotides Having Random Codons at Two Predetermined Positions

In the claims:

89. (Amended) The processed gVIII fusion protein of claim [89] 88, wherein said functional portion of the gVIII fusion protein is encoded by a non-identical copy of gVIII having a nucleotide sequence different than wild type gVIII.

90. (Amended) A filamentous bacteriophage comprising the processed gVIII fusion protein of claim 89 expressed on its surface.